

B18

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>C07C 253/34, 255/23</b>	<b>A1</b>	(11) International Publication Number: <b>WO 96/14292</b> (43) International Publication Date: 17 May 1996 (17.05.96)
(21) International Application Number: <b>PCT/IE95/00053</b> (22) International Filing Date: 18 October 1995 (18.10.95) (30) Priority Data: 940864                      4 November 1994 (04.11.94)    IE (71) Applicant (for all designated States except US): <b>SALDANE LIMITED (IE/IE)</b> ; Molyneux House, Bride Street, Dublin 8 (IE). (72) Inventors; and (75) Inventors/Applicants (for US only): <b>DYATLOV, Valery Alexandrovich (RU/RU)</b> ; Malyl Levshinskyl per. 12-6, Moscow, 119034 (RU); <b>MALEEY, Viktor (RU/RU)</b> ; B.Serpuchovskaya, 70-66, Moscow, 113093 (RU); <b>GU-SEVA, Tatiana (RU/RU)</b> ; Biryulevskaya 45-201, Moscow, 115372 (RU). (74) Agent: <b>ANNE RYAN &amp; CO.</b> ; 60 Northumberland Road, Ballsbridge, Dublin 4 (IE).	(81) Designated States: AM, AU, BG, BR, BY, CA, CN, CZ, DE, EE, FL, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MN, MX, NO, NZ, PL, RQ, RU, SD, SI, SK, TJ, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).  Published With international search report. With amended claims.	
(54) Title: <b>PROCESS FOR THE PURIFICATION OF A NON-ENOLISABLE ESTER WITH A METALLIC REAGENT SELECTED FROM A METAL, A METAL OXIDE OR A METAL HYDRIDE</b>  (57) Abstract  A process for purification of non-enolisable esters, especially esters of 2-cyanoacrylic acid, from contaminating volatile acids, non-volatile acids and other substances which can decompose to generate strongly acidic impurities, comprises reacting a solution of the ester with a metallic reagent selected from a metal, metal oxide and a metal hydride or a mixture thereof in the form of a dispersion, emulsion or suspension. The metallic reagent is optionally supported on a solid, insoluble support. The process is especially suitable for the purification of liquid, non-distillable esters of 2-cyanoacrylic acid.		

BEST AVAILABLE COPY

BEST AVAILABLE COPY

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LJ	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

WO 96/14292

PCT/IE95/00053

1

### Description

PROCESS FOR THE PURIFICATION OF A NON-ENOLISABLE ESTER WITH A METALLIC REAGENT SELECTED FROM A METAL, A METAL OXIDE OR A METAL HYDRIDE

### Technical Field

5 This invention relates to a process for the purification of esters, in particular, esters of 2-cyanoacrylic acid so that they can be obtained uncontaminated by acidic impurities, especially non-volatile acidic impurities.

### Background Art

10 The ability of esters of 2-cyanoacrylic acid to polymerise rapidly (anionic polymerisation) under the influence of moisture or nucleophilic substances has led to their commercial exploitation as instantaneous adhesives. This polymerisation reaction is inhibited by acidic species and such inhibition may be partial or total. Partial inhibition leads to greatly increased setting times for the adhesive  
15 compositions with accompanying loss of industrial usefulness, and total inhibition leads to complete loss of adhesive properties. Very small (p.p.m.) amounts of acidic contaminants are able to cause inhibition of the anionic polymerisation process.

20 Several methods for the preparation of esters of 2-cyanoacrylic acid have been described. Patent Publication WO 94/15907 describes the synthesis of esters of 2-cyanoacrylic acid *via* its direct acid-catalysed esterification wherein a strong, usually non-volatile acid is used as catalyst. Patent Publication WO 94/15907 further describes the synthesis of esters of 2-cyanoacrylic acid *via* reaction of the derived 2-  
25 cyanoacryloyl chloride with, for example, an alcohol. In each instance, the esters of 2-cyanoacrylic acid which are formed may sometimes be contaminated by small amounts of acidic substances sufficient to inhibit their anionic polymerisation reaction to a greater or lesser degree. Such acidic substances may be derived *inter alia* from the strong acid  
30 catalyst mentioned *supra*, from side-reactions which take place during

WO 96/14292

PCT/IE95/00053

2

the preparation of intermediate 2-cyanoacryloyl chloride to give substances which may later release strong acids such as hydrochloric acid, or from residual unesterified 2-cyanoacrylic acid or 2-cyanoacryloyl chloride.

- 5           The extremely low level of acid contamination which can be tolerated when esters of 2-cyanoacrylic acid are to be utilised as instantaneous adhesives means that removal of such contamination is essential. In the case of distillable esters of 2-cyanoacrylic acid this can be achieved by distillation. However, few esters of 2-cyanoacrylic acid  
10       can be purified in this way as esters wherein the esterifying group contains more than about eight carbon atoms suffer decomposition at their boiling points even if the distillation is attempted at reduced pressure. A very large number of esters of 2-cyanoacrylic acid fall into this category. In the case of solid esters of 2-cyanoacrylic acid,  
15       recrystallisation may sometimes be used as a method for their purification. This is not always convenient as large volumes of solvent may be required. The use of basic substances for the removal of acidic contaminants from esters of 2-cyanoacrylic acid has not been utilised hitherto due to the instantaneous polymerisation reaction which these  
20       esters undergo upon their exposure to nucleophilic species.

Thus, a process for the removal of acidic contaminants, especially non-volatile acidic contaminants, from liquid, non-distillable esters of 2-cyanoacrylic acid has not yet been described.

- 25           However, a process for the removal of acidic contaminants, especially non-volatile acidic contaminants, from non-enolisable esters, generally and esters, including distillable and solid esters, of 2-cyanoacrylic acid in particular, is required which overcomes the aforementioned problems associated with known processes for their purification.

30

WO 96/14292

PCT/DE95/00053

3

### Disclosure of Invention

Accordingly, there is provided a process for the purification of non-enolisable esters from contaminating volatile acids, non-volatile acids and other substances which can decompose to generate strongly acidic impurities, which comprises reacting a solution of said ester with a metallic reagent selected from a metal, a metal oxide and a metal hydride or a mixture thereof in the form of a dispersion, emulsion or suspension, said metallic reagent optionally being supported on a solid, insoluble support.

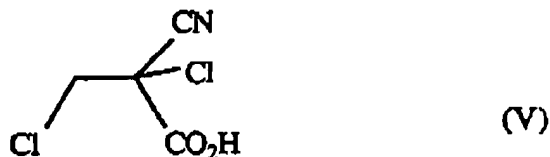
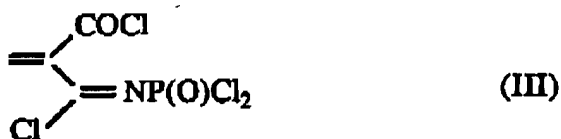
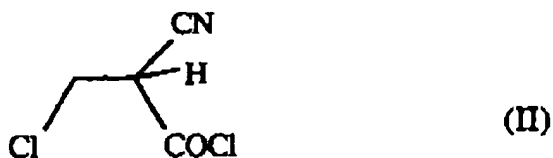
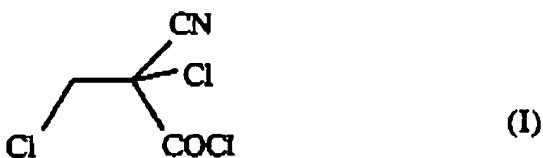
By volatile acid herein is meant any acid which can be largely, but not completely, removed by sparging with an inert gas, by heating or by pumping under reduced pressure.

By non-volatile acid herein is meant any acid or polyacid which cannot be removed by sparging the reaction mixture with an inert gas under any reasonable conditions of temperature and pressure. Examples of such non-volatile acids include, but are not limited to, alkyl- or arylsulfonic acids which may be employed as catalysts for the direct esterification of 2-cyanoacrylic acid. Further examples include, but are not limited to, phosphoric acid, polyphosphoric acid or halo-derivatives thereof which may be formed as by-products during the preparation of 2-cyanoacryloyl halides from 2-cyanoacrylic acid by reacting the latter with a phosphorus halide, especially with phosphorus tri- or pentachloride to yield 2-cyanoacryloyl chloride. Additional examples of non-volatile acids include substances such as those indicated in formulae (I)-(V):

WO 96/14292

PCT/IE95/00053

4



5 which may be formed from 2-cyanoacrylic acid as by-products during its conversion to 2-cyanocryloyl chloride by reaction with a phosphorus chloride.

Compounds of types (I)-(III) may, on storage, liberate hydrochloric acid. Compounds (IV) and (V) are capable of both releasing hydrochloric acid and of acting as strongly acidic inhibitors in their own right.

WO 96/14292

PCT/IE95/00053

5

Preferably, the ester is an ester of 2-cyanoacrylic acid, more especially a liquid, non-distillable ester.

The invention will be described hereinafter with particular reference to esters of 2-cyanoacrylic acid.

5           According to one aspect of the invention the metallic reagent used for removing contaminating acidic species from esters of 2-cyanoacrylic acid can be a suspension of a metal in an inert organic solvent and in the absence of a solid, insoluble support. The metal can be an alkali, alkaline earth or transition metal. Preferably, the metal can  
10       selected from lithium, sodium, potassium, calcium, aluminium and iron. The inert organic solvent is suitably any dry inert solvent, especially hexane, toluene or benzene.

15           For example, as is well known, finely-divided suspensions of potassium in benzene or of sodium in toluene can be prepared by melting these metals in boiling solvent, stirring vigorously to generate an emulsion, and then cooling the mixture to give the required suspension of solid metal.

20           In another aspect of the invention, the metallic reagent is a suspension of a metal oxide or of a metal hydride in an inert organic solvent which can be used to remove acidic contaminants from esters of 2-cyanoacrylic acid. The inert organic solvent is suitably any dry inert solvent, especially hexane, toluene or benzene. Suitably, the metal oxide is the dry oxide of an alkali, alkaline earth or other metal. Examples include, but are not limited to, magnesium oxide, calcium  
25       oxide and aluminium oxide.

30           Suitably, the metal hydride is the hydride of any alkali, alkaline earth or other metal, such hydride being unable to chemically reduce any unsaturated linkages present in said esters either in the carboxylic moiety or in the esterified radical. In a preferred embodiment of this aspect of the invention the metal hydride is calcium hydride.

WO 96/14292

PCT/IE95/00053

6

In a further aspect of the invention a solid, insoluble support is used to carry the metal, metal oxide or metal hydride or mixture thereof utilised to remove contaminating acidic impurities from esters. The support may take the form of either an inert or a reactive support.

5 By inert support herein is meant any supporting medium able to carry by adsorption a metal, metal oxide or metal hydride as defined *supra*, but which is unable to react with said metal, metal oxide or metal hydride.

10 By reactive support herein is meant a supporting medium which is able to react with the metal, metal oxide or metal hydride to form a new chemical species which then operates to remove the contaminating acidic impurities.

15 The choice of supporting medium depends upon the type of metal, metal oxide or metal hydride which is being used. Typical supports include, but are not limited to, powdered charcoal, aluminium oxide, silicon oxide and aluminosilicates. Some of these supports may behave either as inert or as reactive supports depending upon the nature of the metal, metal oxide or metal hydride which is adsorbed thereon. For example, charcoal behaves as an inert support towards iron oxide  
20 but as a reactive support towards potassium with which it forms an inclusion compound. A metal oxide can be utilised as a reactive support. For example, calcium oxide can be treated with a limited amount of sodium metal to provide *via* a metathesis reaction calcium oxide carrying a mixture of sodium oxide and calcium metal. Thus, a  
25 solid support may be freed from residual moisture and then loaded with a metal, a metal oxide, a metal hydride or a mixture of metal(s) and metal oxide(s).

30 Optionally, the metal is applied to the surface of the support by chemical reduction of a metal oxide which forms the support or which has been applied to the surface thereof. Layers of metal oxides can be applied to the surface of a support by thermal breakdown of an appropriate salt adsorbed thereon. For example, a layer of iron oxide



WO 96/14292

PCT/IE95/00053

7

can be deposited on powdered aluminium oxide by coating the latter with iron nitrate and then heating the product.

5 The ester to be purified according to the invention may be dissolved in an inert organic solvent such as hexane, benzene or toluene. Alternatively, esters prepared in such solvents by the acid-catalysed esterification of a carboxylic acid or by reaction of an acyl halide with an alcohol or phenol can be purified in solution without evaporation of the solvent and intermediate isolation of contaminated ester. These solutions may optionally contain a stabiliser which inhibits  
10 the anionic polymerisation, a stabiliser which inhibits the free-radical polymerisation or a mixture of such stabilisers. However, the presence of a stabiliser is not essential.

15 When esters of 2-cyanoacrylic acid are to be purified according to the process of the invention the presence of a mixture of stabilisers which inhibit anionic and free-radical polymerisation reactions is preferred. These inhibitors must themselves be stable under the conditions of the purification process. The most preferred types of anionic polymerisation inhibitors are sulfonic acid esters, and the most preferred types of free-radical polymerisation inhibitors are  
20 appropriately substituted esters of 2-cyanoacrylic acid. By appropriately substituted ester in this context is meant a substituted ester effective to achieve the requisite inhibition.

25 The purification step according to the invention is carried out by vigorously mixing a solution of the ester to be freed from acidic contaminants with an emulsion, suspension or dispersion of one of the metallic reagents hereinabove described.

Suitable inhibitors of anionic and free-radical polymerisation reactions may first be added to the solution when polymerisable esters such as esters of 2-cyanoacrylic acid are to be purified.

30 Preferably, the mixture is sparged with a dry inert gas such as nitrogen, argon or helium before and during the purification process in

WO 96/14292

PCT/IE95/00053

8

order to remove any volatile acids which may be present. The temperature at which the purification process is carried out depends upon the nature of the ester to be purified, the solvent used, and the nature of the metallic reagent used. The process according to the invention can be carried out at temperatures between  $-20^{\circ}\text{C}$  and  $150^{\circ}\text{C}$ , preferably between  $+20^{\circ}\text{C}$  and  $110^{\circ}\text{C}$ . The purification of esters containing chemical functionality which is prone to free-radical polymerisation can be carried out at  $20^{\circ}\text{C}$ – $40^{\circ}\text{C}$  in order to prevent thermally-induced free-radical polymerisation reactions from taking place. When thermally stable esters are being purified by the process according to the invention wherein an alkali metal such as sodium is the metallic reagent then it is preferable to conduct the process at a temperature higher than the melting point of the metal, so that an emulsion of molten metal is present.

The duration of the purification process according to the invention depends upon the level of acid contamination initially present in the ester, the temperature at which the purification is carried out, and the nature of the metallic reagent used for purification.

Initial sparging with an inert gas as described *supra* removes much of any volatile acid contamination which may be present, and this reduces the time needed to complete the purification process.

In the case of esters of 2-cyanoacrylic acid which polymerise by the anionic polymerisation process, the progress of the purification reaction can be monitored by measuring the setting time of the isolated ester needed to give a satisfactory adhesive bond.

The isolation of purified ester from the reaction mixture is preferably carried out by cooling to ambient temperature, removal of the metallic reagent by filtration or centrifugation, and evaporation of the solvent under polymerisation-inhibiting conditions.

For liquid esters of 2-cyanoacrylic acid, anionic polymerisation can be inhibited by the addition of non-volatile stabilisers additional to